Original Article

Robotic radical cystectomy for the management of bladder cancer: Analysis of operative and pathological outcomes of eighteen patient

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ABSTRACT

Objective: To present the surgical and pathological results of robotic radical cystectomy (RRC) operations performed in our clinic.

Material and methods: A total of 18 patients, who underwent RRC and intracorporeal urinary diversion between October 2016 and September 2017 for clinically localized bladder cancer in our clinic, were included in the study. The results were evaluated under three headings. 1. operative outcomes (total operation time, perioperative blood loss, postoperative hematocrit decrease) 2. recovery period (pull-off drain day, hospitalization time) 3. oncological results (pathologic stage, surgical margin, number, and characteristics of lymph nodes removed). Complications within the postoperative 30-day period, were evaluated and the Clavien classification system was used to classify the complications.

Results: The mean age of the patients was 64.4 (52-80) years. Seventeen male patients and one female patient underwent robotic cystectomy. At the operative outcomes, the mean blood loss was 325 mL, and the mean hematocrit decrease was 3.15%. The mean duration of the surgery was 471 minutes (330-630), while the median operative time was 450 minutes. Complications occured in 6 patients during the early postoperative period. Six of them (75%) had minor complications (Clavien grade 1), two patients (25%) had major complications (Clavien grade 4).

Conclusion: Our initial experience with RRC is that, this surgical technique has acceptable operative, oncological and short-term clinical outcomes. However, prospective randomized studies are needed to assess whether there is a clear advantage compared to open surgery.

Keywords: Bladder cancer; complication; cystectomy; robotic.

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Introduction

Radical cystectomy is still the most effective treatment modality for muscle-invasive or high risk non-muscle invasive bladder tumors with respect to local control, and disease-free survival, and it may be recommended for every patient with low comorbidity index irrespective of patient's age.[1,2] As an alternative to open surgery, laparoscopic cystectomy performed for a patient with neurogenic bladder was firstly reported by Parra et al.[3] in the year 1992, and in following years the experiences of laparoscopic cystectomy were shared in parallel with development of laparoscopic techniques.[4] After accumulation of experience in laparoscopic surgery, the first robot-assisted radical cystectomy was described, and realized by Menon et al. in the year 2003.[5] Thanks to its lesser morbidity with better oncological, and functional results robotic radical prostatectomy has been started to be used prevalently. Besides in line with accumulating experiences in robotic surgery, first publications were released about robotic radical cystectomy (RRC).[6,7] In series of RRC published in the following years, the authors reported lesser blood loss, faster recovery of bowel movements, and earlier discharge, and because of these reasons RRC has been

accepted as a successful treatment modality.[8,9] In recent years positive effect of extended pelvic lymphadenectomy on survival has been demonstrated which focused attention on this issue, and the centers with heavy patient circulation have proposed their own standards for this procedure. As has been suggested at least 10-14 lymph nodes should be sent for histopathological examination, the most important issue has been indicated as being the uppermost level of dissection rather than the number of lymph nodes removed.[10,11]

Though in recent years robotic surgery has been widely used in Turkey, only a few studies on RRC have been published so far. Atmaca et al.[12] compared RRC, and open cystectomy series, and indicated improved oncological, and functional outcomes in robotic surgery. They also demonstrated superiority of RRC in terms of lymph node dissection, blood loss, and duration of hospitalization. Herein we aimed to contribute to the literature by reporting our preliminary experiences in robotic RRC, its perioperative outcomes, and histopathological results.

Material and methods

Eighteen patients diagnosed as clinically localized bladder tumor, and underwent RRC, and intracorporeal urinary diversion between October 2016, and September 2017 in our clinic were included in the study. Our first experience with robotic cystectomy was gained with these 18 patients. Preoperatively all patients underwent the following tests, and examinations: whole blood cell counts, extended blood biochemistry, bleeding time, contrast-enhanced thoracic, and abdominopelvic computed tomography. Excluding the patients suspected of having metastasis, positron emission tomography (PET) was not routinely used. Two patients evaluated preoperatively in the uro-oncology council, and then received cisplatin-based neoadjuvant chemotherapy.

All patients were started on liquid diet one day before the surgery. Mechanical bowel preparation was performed with Fleet Fosfo–Soda given the night before the operation, and on the morning of surgery Fleet enema was applied. The patients underwent radical cystoprostatectomy, extended pelvic lymphadenectomy, and intracorporeal urinary diversion using da Vinci Xi robotic system. Cystoprostatectomy was performed using the method described by Wang et al.[13]. Obturator, external iliac, hypogastric, and sacral lymph nodes were removed during lymphadenectomy. As diversion procedures, for the construction of neobladder Studer's, and for ileal diversion Bricker's techniques were used. After routine procedures performed by anesthesia clinic, the patient was brought into postoperative intensive care unit. The patients with stable health state were transferred into the service on the first postoperative day. The patients whose nasogastric tubes were drawn at postoperative

12 hours, were urged for early mobilization, and gradually oral intake was initiated.

The results were evaluated under three headings. 1) Surgical outcomes (total operative time [cystectomy, bilateral pelvic lymphadenomectomy, urinary diversion], perioperative blood loss, postoperative decrease in hematocrit) 2) Recovery period (day of drain removal, duration of hospitalization) 3) Oncological outcomes (pathological stage, surgical margins, number, and characteristics of the removed lymph nodes). Complications developed within postoperative 30 days were evaluated. For the classification of complications, Clavien classification system which ensured standardization in urology practice, and used in many literature studies for evaluation was employed.

Written informed consent of each patient was obtained, and our study was conducted in compliance with Helsinki Declaration. Since it was a retrospective study, ethics committee approval was not obtained.

Statistical analysis

Basic and descriptive statistical analysis have been used in this study and all data were expressed as mean, median (minimum, maximum) for numerical variables; as frequencies and percentages for categorical variables.

Results

Median age of the patients was 64.4 (52-80) years. RRC was performed for 17 male, and one female patient. Patients were operated with the diagnosis of cT1 (3/18; 16.7%), and cT2 (15/18; 83.3%) bladder tumor. As urinary diversion intracorporeal ileal loop (n=7), and intracorporeal orthotopic neobladder (n=9), and ureterocutaneostomy (end-stage renal failure) were realized. Patient characteristics are shown in Table 1.

Average blood loss was 325 mL (median, 300 mL), average drop in hematocrit was 3.15% (median, 2.17%). Average (471: 330-630 mins), and median (450 mins) operative times were calculated. As recovery time results, median drain removal, and discharge times were determined as 10., and 12. postoperative days, respectively (Table 2).

During early postoperative period (the first postoperative 30 days) complications developed in 8 patients. These were either minor (Clavien grade ≤2; n=6; 75%) or major complications (Clavien grade ≥3; n=2; 25%). None of the patients were lost because of reasons related to surgery or its complications. All complications, and their grades are shown in Table 3.

According to histopathological test results of specimens, surgical margin positivity was not detected in any patient. On an average 14 (8-30) lymph nodes were resected, and in 5 patients lymph

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node positive disease was detected. Organ-confined disease (≤pT2) (61%), pT3 (6%), pT4 (prostatic invasion), and lymph node positivity (pTxN+) were detected in respective percentage of patients. Pathologic stages of lymph node positive patients were classified as follows: pT2 (40%), pT3 (40%), and pT4 (20%).

Table 1. Patient characteristics

Variable	Result
Age (mean) years	64.4 (52-80)
Gender, n	
Male	17
Female	1
Clinical stage, n (%)	
cT1	3 (16.7%)
cT2	15 (83.3%)
Type of diversion, n (%)	
Ileal loop	7 (39%)
Neobladder	9 (50%)
Ureterocutaneostomy	2 (11%)

Table 2. Surgical outcomes

Variable	Median	Median
Operative time, min	471 (330-630)	450
Blood loss, mL	325 (175-550)	300
Drop in hematocrit, %	3.15 (2-4.9)	2.7
Hospital stay, days	14.7	12

Average (range) duration of clinical follow-up period was 8.9 (6-16) months. Five (27%) patients who were referred to oncology unit because of lymph node positivity were given cisplatin-based chemotherapy as adjuvant therapy. One (5%) of these patients was lost because of pancytopenia developed secondary to chemotherapy at 8. postoperative month. Any evidence of distant metastasis was not detected in PETs obtained for the other 4 patients who completed adjuvant chemotherapy cures. Radiological examinations of 13 patients performed at postoperative 6. months did not reveal any local recurrence or distant metastasis.

Discussion

Radical cystectomy is still accepted as the gold standard treatment modality in muscle-invasive, recurrent, high-risk bladder tumors.[14] Within the last 10 years many articles have been published by various clinics about applicability, and reliability of RRC.[15,16] With accumulation of experience, robotic cystectomy has been modified many times, and its use in neurological, prostate, vagina-sparing surgery, and also in total intracorporeal diversion techniques have been described.

In our country, robotic surgery has been widely used in recent years which shortened previously long-lasting learning curve of laparoscopy in abdominal, and pelvic surgery. Improved delineation of anatomic structures thanks to increased use of robotic radical prostatectomy, and increased experience in pelvic surgery have encouraged the surgeons to perform robot-assisted techniques for cystectomy. We also shared our results of RRC which we started to perform after our experience we gained from robotic radical prostatectomes we realized in 103 patients in our clinic. It is noteworthy to indicate that two surgeons who performed RRCs have an ample experience in laparoscopic interventions.

Table 3. Complications and Clavien grades

Complication	n	Clavien grade	Approach
Ileus	1	2. grade	Ileus developed on postoperative 17. days was relieved with conservative surveillance
Urinary system infection	2	2. grade	Parenteral antibiotherapy was used because of development of complicated urinary infection on postoperative 20., and 24. days
Blood transfusion	2	2. grade	On postoperative 1. day 2 patients were given one unit erythrocyte suspension
Ureteroileal anastomotic leak	1	3. grade	Bilateral nephrostomy tubes were placed because of urine leak discerned on postoperative 10. day, and surgical intervention was not required
Catheter removed accidentally	1	1. grade	Conservative follow-up for accidentally removed ureter catheter on postoperative 3. day.
Neobladder rupture	1	4. grade	Surgical intervention was performed for acute abdomen developed secondary to rupture of the neobladder on postoperative 25. day.

In consideration of perioperative outcomes, our operative time was slightly longer relative to the operative times reported in the literature. As reported by Hayn et al.[17] 21 patients should be operated to achieve an operative time of 6.5 hours, and 30 patients should be operated to complete a learning curve for 20 lymphadenectomies, and in this study extracorporeal urinary diversions were performed. In a series of 132 patients who had undergone intracorporeal diversion an average operative time of 7.6 hours was reported.[18] As is the case in every surgical intervention, we think that our operative time in RRC will decrease in parallel with the increase in the number of our patients. In various series lesser amount of perioperative blood loss, and decrease in hematocrit levels were indicated when compared with open surgery with an average blood loss ranging between 273, and 473 mL.[19,20] In our series average blood loss was 325 mL, and drop in hematocrit was 3.15% which were within acceptable limits.. As for hospital stays, we think that for a major surgery 12 days should not be considered as a prolonged hospital stay, and as experiences accumulate, lymphatic drainage which develops after lymphadenectomy may be prevented, and drain withdrawal, and discharge times may be performed at an earlier date. Therefore conduction of a randomized study which will compare open, and robotic surgery will be more appropriate.

Complications developed in 8 (44%) patients most of them (75%) being minor complications. Generally our low rate of complications was at an acceptable level, and also comparable to that of our series.[17-20] In one patient neobladder rupture (Clavien grade 4) developed on postoperative 25. day. The patient was explored, and any problem in the perfusion or blood supply of the neobladder was not observed. A punctured site on the right lateral wall of the bladder which was thought to be related to perforation occurred probably during clean intermittent self-catheterization was detected, and the defect was primarily repaired.

We think that robotic surgery observes oncological criteria with acceptable pathological outcomes based on our evaluation of its oncological results. It should not be forgotten that lack of any surgical margin positivity in any patient may be related to higher surgical success rates, and also appropriate patient selection for our preliminary case series. As reported in the literature, as the number of operated cases increases, RRC's can be performed for more bulky tumors with clinical stage T3 without compromising favourable oncological outcomes.[17] Pelvic lymphadenectomy which is an important component of RRC can be easily accomplished using robot-assisted technique. Lymph node positivity detected in our 5 patients may indicate superiority of robotic surgery related to this issue. Preoperative radiological examinations did not reveal any pathologically enlarged lymph nodes in 4 out of 5 patients. PET was obtained for one patient who had an enlarged paraaliac lymph node

without any significant involvement. As indicated in various publications, PET scans provide better visualization of anatomic sites, and facilitates especially removal of presacral (in case of need paracaval, paraaortic) lymph nodes.[21] In a cadaver study, 10-53 (median 8) pelvic lymph nodes were detected in patients who had previously undergone extended PLND. The authors indicated that upper level of dissection was more important than the number of lymph nodes removed.[22] In another publication, Roth et al.[23] dissected 13-72 lymph nodes using standard PLND. Canda et al.[24] indicated that they dissected an average of 24 lymph nodes in their series. As is understood, number of lymph nodes excised differ individually in every patient, and the upper level of dissection carries importance. We removed an average of 14 (median, 18) lymph nodes. The number of lymph nodes we removed increased in parallel with the number of cases. We think that the number of lymph nodes may change since pathologists did not prepare slides from impalpable lymph nodes, and specimens were not examined by a single pathologist. As demonstrated in many studies use of cisplatin-based neoadjuvant chemotherapy provided a 5% advantage in 5-year survival rates which encouraged its use in urology clinics.[25] In the United States of America NAC was used in 20.9% of the cases in the year 2010, while it has been used in 12-29%+ of the patients.[12,24,26] Since most of our patients had local disease, NAC was used in 11% of our patients. However our use of NAC will increase in line with increase in the number of our patients with locally advanced disease.

Most important limitations of our study are scarce number of our patients, and lack of our cancer-related long-term results encompassing a total of 2 or preferably 5 years. Besides in this study, data collected by two separate surgeons were evaluated in combination which may effect surgical, and oncological results. This study does not give an explicit response to the most important question in our mind ie." Does robotic cystectomy provide a clear advantage over open surgery?" Prospective, randomized studies to be performed on this subject will respond the questions in our mind more precisely.

In conclusion, our preliminary experiences with RRC have indicated that this surgical technique has acceptable surgical, oncological, and short-term clinical outcomes. As experiences with robotic surgery accumulate, we think that more improved results will be obtained in parallel with the development in surgical technique. However assessment of any clear-cut advantage of RRC (if any) relative to open surgery requires realization of further prospective randomized controlled studies.

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Informed Consent: Written informed consent was obtained from patient who participated in this study.

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